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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/918,187	07/30/2001	Rosanne M. Crooke	ISPH-0590	2706

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EXAMINER	
LACOURCIERE, KAREN A	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 06/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/918,187	CROOKE ET AL.	
	Examiner	Art Unit	
	Karen A. Lacourciere	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-15 and 21-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-15, 21-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-7, 9, 10, 12, 13, 14 and 15 are maintained as rejected under 35 U.S.C. 102(b) as being anticipated by Damha et al. (WO 99/67378), for the reasons of record set forth in the prior Office action mailed 10-23-2003).

Response to arguments

Applicant's arguments filed 03-24-2004 have been fully considered, but have not been found to be persuasive. In response to the rejection of record, Applicant argues that the amended claims require the length of the antisense sequence be between 17 and 50 nucleobases long and, therefore, Damha does not met the limitations of the claims as only 15 residues occur in the antisense sequence. This has not been found to be persuasive because the claims limit the length of the antisense compound to at least 17 residues, rather than the antisense portion. Therefore, including the 18-mer antisense compound disclosed by Damha et al. meets the length limitation of the amended claims.

Claims 1, 4-6, 10, 12, 13, 14, 15 and 21 are maintained as rejected and new claims 22 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by

Beigelman (WO 96/18736) for the reasons of record set forth in the prior Office action, mailed 10-23-2003.

Applicant's argument filed 03-24-2004 have been fully considered, but have not been found to be persuasive. In response to the rejection of record, Applicant argues that the amended claims require that the antisense sequences fully hybridize, e.g. 100%, with the target and that the ribozyme disclosed by Beigelman includes non-hybridizing residues.

This is not found to be persuasive because the amended claims include a limitation that the compound fully hybridize to the target, which does not limit the claimed compound to one wherein the full length of the compound is 100% complementary to the target. Given the region of complementarity of the ribozyme taught by Beigelman to the target sequence it would be expected that the ribozyme would "fully hybridize" to the target.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 4-10, 12-15 and 21 are maintained as rejected and claims 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stenn et al. (WO 00/09754, cited on PTO form 1449, filed June 4, 2002) in view of Milner et al. and Baracchini et al. (US Patent No. 5,801,154) for the reasons of record set forth in the prior Office action.

Response to Arguments

In response to the rejection of record under 35 USC 103(a), Applicant argues that there is no reasonable expectation from the cited reference Stenn et al. or the secondary references that the skilled artisan would be able to find antisense sequences that inhibit the expression of stearoyl-CoA desaturase to any degree. These arguments have been considered, but are not found to be persuasive.

Applicant argues that the skilled artisan would not reasonably expect to find antisense sequences that inhibit the expression of stearoyl-CoA desaturase by 50%, however, Applicant is arguing a limitation that is not found in the claims. The claims are directed to inhibition of at least 10%, which is a very low degree of inhibition, and can occur under generally any assay conditions.

Applicant argue that Stenn et al. does not say anything about antisense

sequences, however, Stenn et al. does discuss inhibition of stearoyl-CoA desaturase using antisense and includes an embodiment wherein a full length antisense sequence is used to inhibit stearoyl-CoA desaturase. Applicant argues that Baracchini et al. demonstrates that in a test of 16 antisense compounds only one exhibited greater than 30% inhibition and one other inhibited to greater than 95% and that Baracchini et al. is silent with regard to the level of inhibition of the other oligos tested. Applicant argues that Milner et al. provides similar evidence, wherein three oligos tested against a target produced inhibition of expression levels by 0%, 36% and 100%. Applicant argues that given the data in the cited references, there would be no expectation as to a level of inhibition would be achieved using antisense sequences. This has not been found to be persuasive because the cited references demonstrate even testing a small number of antisense sequences the skilled artisan would be expected to find at least one oligonucleotide that inhibits to a level of greater than 10%. Reading further in Baracchini, it is clear that the additional oligonucleotides tested also exhibit high levels of inhibition, based on the data presented that show significant tumor size reduction using these oligos. Further, Baracchini et al. also discuss (column 11) how the oligos shown to inhibit by 95% and 36% in one assay, could be shown by Northern blot to inhibit expression entirely under other conditions. Additionally, reading Milner et al. more closely, in Table 1 the reference demonstrates that in testing five different oligonucleotides targeted to rabbit B-globulin, found using the array method taught by Milner et al., all five of the oligos inhibited the expression of the target by greater than 50%, once the assay conditions were adjusted. Milner et al. states that their empirical

method can be used to find effective antisense to any target RNA of known sequence. In each both Baracchini et al. and Milner et al., multiple oligonucleotides could be found that inhibited the expression of a target gene, even if every single complementary oligonucleotide was not expected to be as effective. Considering the references cited, the skilled artisan would reasonably have expected to find at least one antisense oligonucleotide that inhibited the expression of stearoyl-CoA desaturase by at least 10% under some assay condition by screening for antisense against the known sequence, as claimed.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 USC 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-7, 9, 10, 12-15, 21 and 22 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

In the amendment filed 03-24-2004 the new limitation wherein the claimed antisense is 17 to 50 nucleobases in length has been added to claim 1 and the limitation wherein the claimed antisense is 19 to 50 nucleobases in length has been added to

claim 22. No support for the lower limitations of 17 and 19 nucleobases could be found in the originally filed specification or claims. Applicant points to the specification at page 83 and 84 to support these lower limitations, however, support for the newly claimed range could not be found on page 83 or 84. Although there are two oligonucleotides, SEQ ID NO: 4 and 7, these oligonucleotides are disclosed as PCR primers and probes. The specification does not suggest making antisense compounds with a lower length limitation of 17 or 19 nucleobases, the two PCR primer disclosed do not provide support for these new limitations.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP §706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Lacourciere whose telephone number is (571) 272-0759. The examiner can normally be reached on Monday-Thursday 7:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Lacourciere
June 7, 2004

Karen A. Lacourciere
KAREN A. LACOURCIERE, PH.D
PRIMARY EXAMINER